

# Accidental Intramuscular Vincristine: Lack of Untoward Effects and Recommendations for Management

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Vincristine was inadvertently injected into a thigh of three children. In each case the accident occurred as a result of the mixing of a syringe containing vincristine with a syringe of L-asparaginase which the patient was scheduled to receive on the same day. Within minutes, each patient was treated topically with cold compresses and the area was infiltrated with a solution of 8.4% sodium bicarbonate. Only one patient had discomfort of the thigh after the injection, none of the patients have had any sequelae, either acute or delayed.

Measures to avoid mistaken injection of vincristine for asparaginase are readily achievable and have prevented recurrences of intramuscular vincristine administration at the institutions where they have been implemented. Nonetheless, other instances of intramuscular vincristine injection are anticipated and should be rapidly recognized and quickly managed with local applications of cold and sodium bicarbonate. *Med. Pediatr. Oncol.* 28:314–315.

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## INTRODUCTION

Most induction regimens for acute lymphoblastic leukemia include both vincristine and L-asparaginase therapy. The vincristine must be given intravenously and the asparaginase is usually administered intramuscularly. Ordinarily four doses of vincristine are administered at weekly intervals and nine doses of L-asparaginase are given at 2–3 day intervals. Over a course of induction therapy for acute lymphoblastic leukemia, two or three doses of L-asparaginase are usually injected intramuscularly on the same day that vincristine is administered. Because the volume of injection and the syringes used for the two drugs are similar, the syringes may be inadvertently switched and the vincristine administered intramuscularly.

We know of three patients who received intramuscular vincristine under these circumstances. In each instance, the misadventure was recognized immediately and, with minimal intervention, the outcome was benign. Despite expectation of deep tissue necrosis, clinical significant sequelae were not observed. In this communication, we report the circumstances, the minimal initial management and long-term follow-up of the three patients. To help prevent occurrence elsewhere, we also offer a few recommendations for prevention.

## CASE REPORTS

### Case 1

An 8-year-old boy with newly-diagnosed acute lymphoblastic leukemia was in the hospital being induced into remission with weekly vincristine, daunomycin, and

daily prednisone, three-times-weekly L-asparaginase and a high-dose of methotrexate infusion with leucovorin rescue. On the 18th hospital day he received 1.0 mg vincristine sulfate (Oncovin, Lilly Laboratories), in a volume of 1.0 ml, intramuscularly into his right anterior thigh. The error was recognized immediately and cold compresses were applied to the area. Within about 20 minutes 5.0 ml of 8.4% sodium bicarbonate was infiltrated locally into the area of the injection. Warm packs were then applied for 1 hour, followed by cold packs applied for an unknown period of time.

Later that day a bruise was noted at the injection site, but there was no discernible erythema or warmth and the patient did not complain of pain. The next day, however, and intermittently for up to 6 days after the injection, pain was noted and treated with cold or warm compresses. Throughout, the patient was able to bear weight on the extremity and walked normally. At no time was there induration, erythema, swelling or tissue breakdown. The patient died of generalized leukemia 4.5 years later, and no perceptible residual effect was noted. An autopsy

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was performed at another institution. The extremities were noted to be unremarkable.

## Case 2

This 9-year-old girl was on maintenance therapy for acute lymphoblastic leukemia when she received a dose of intramuscular vincristine. This incident occurred in the outpatient department on a day when she was due for intravenous vincristine and intramuscular L-asparaginase. Both syringes were placed on the same tray and brought into the therapy room. The syringe containing 1.1 mg of vincristine (Oncovin, Lilly Laboratories) in 1.1 ml was picked up instead of the L-asparaginase syringe and injected intramuscularly into the left anterior thigh. The error was immediately recognized and ice was applied to the injection site for five minutes. Hydrocortisone 50 mg in 1.0 ml and sodium bicarbonate 5.0 ml of 8.4% were infiltrated deep into the intramuscular site of the vincristine injection. Warm compresses were then applied over the area for 30 minutes.

During the next two days, moderate pain was noted intermittently at the injection site. Some tenderness was noted upon palpation of the injection site, but there was no induration, erythema, swelling, tissue breakdown, or lower extremity weakness. Complete resolution of the pain and tenderness was noted three days after injection. When last examined 4 years later there was no observable difference in strength or circumference of the thighs.

## Case 3

A 10-year-old boy with acute lymphoblastic leukemia was due for intramuscular asparaginase, intravenous adriamycin, and intravenous vincristine as part of a second course of delayed intensification therapy. The vincristine (1.6 mg, Oncovin, Lilly Laboratories) was administered first, and accidentally injected into the right anterior thigh. The mistake was immediately recognized, and treated locally with cold compresses and within approximately 20 minutes 5.0 ml of 8.4% sodium bicarbonate was infiltrated locally into the area of the injection. Warm packs were applied for one hour, alternating with cold packs for several hours. The asparaginase and adriamycin were withheld, and the dexamethasone which the patient was taking daily, was tapered over the next week.

Later that day, the patient complained of pain at the injection site. Examination revealed some tenderness of the thigh to deep palpation, but no swelling, erythema, warmth, sensory dysfunction, or motor loss. Deep tendon reflexes had been previously obliterated by prior vincristine therapy, with approximately 16 prior doses. The tenderness and pain resolved completely within four days after injection. The patient continues in complete remis-

sion three years after the event, and two years off treatment. He has no motor or sensory abnormalities of the lower extremities and the circumference of the thighs are equal and normal.

## DISCUSSION

In a review of the literature, none of the errors involving pediatric patients receiving chemotherapy included intramuscular vincristine [1]. Fortunately, no untoward sequelae were noted in three patients accidentally injected into the thigh with vincristine sulfate. Whether this favorable outcome was due to topical application of cold and warm compresses and the intramuscular bicarbonate injections each patient received, this however, cannot be determined. Reports on the efficacy of these modalities in the treatment of vincristine extravasation are conflicting. Alternative approaches have included hyaluronidase applied topically or injected locally [2], and warm compresses [3]. These interventions may have been of no specific benefit and the outcome may have been favorable without them. The quadriceps abundant blood supply may also have helped remove the drug from the extravascular compartment rapidly enough to prevent local tissue necrosis. Nonetheless, we recommend that cold applications be applied immediately and that sodium bicarbonate, 8.4%, be injected into the administration site as soon as possible, since all three patients were treated in this fashion and all did well.

In any event, we have instituted changes in our chemotherapy administration policies in an attempt to prevent similar accidents. At one of our centers, medications are now sent by the pharmacy to the inpatient and outpatient units with labels that have different colors for vincristine and L-asparaginase, and both syringes are put in separate places in the treatment room. At all of our centers, each syringe is checked by two different members of the staff prior to administration. To our knowledge, there have been no recurrences of accidental intramuscular vincristine injection at the centers where these policies were instituted.

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